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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,516	03/17/2004	Stewart Loh	RFSUNY-3681 R1407	3967

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EXAMINER

WHALEY, PABLO S

ART UNIT PAPER NUMBER

1631

DATE MAILED: 05/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/802,516	Applicant(s) LOH ET AL.	
	Examiner Pablo Whaley	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 7 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8, 9, and 10-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>03/17/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

APPLICANTS' ELECTION

Applicants' election without traverse of Group I drawn to Claims 1-11 and election of Species A drawn to "ligand binding" and "pH", and Species B drawn to "folded conformations", filed 01/25/2006, is acknowledged. The specie election drawn to Species A is hereby withdrawn for the expedience of prosecution. Claims 7 and 12 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/25/2006.

CLAIMS UNDER EXAMINATION

Claims herein under examination are Claims 1-6 and 8-11.

INFORMATION DISCLOSURE STATEMENT

The information disclosure statement filed 03/17/2004 has been considered in full.

OBJECTIONS

The disclosure is objected to because of the following informalities: (i) The "Detailed description of the invention" does not include a description for Fig. 1B, #25 [p.10]. (ii) The specification contains a hypertext link [p.6]. Appropriate correction is required.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 and 8-11 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. Claim 1 is directed to a "model" for a mutually exclusive folding domain molecular switch. A model, per se, is not a physical product or method, and therefore is not statutory subject matter. Furthermore, because of the conflicting claim language between claim 1 and claims 2-6 and 8-11, which appear to claim "fusion proteins", the examiner has interpreted these fusion proteins be "virtual" proteins. As neither a model nor a virtual protein are physical products or methods, claims 1-6 and 8-11 are not statutory subject matter. See the Guidelines for Patent Eligible Subject Matter (USPTO, 1300 OG 142, Nov. 22, 2005).

CLAIM REJECTIONS - 35 USC §112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-6, 8, 9, and 10-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mutually exclusive folding of a ubiquitin-barnase fusion protein, does not reasonably provide enablement for any other fusion protein comprising insert proteins associated with free energy and target proteins with complex surface loops. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case are

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discussed below which leads to the determination that the above claim lacks enablement due to undue experimentation being required to make and use the invention.

In the instant case, the claimed subject matter lacks enablement for the following reasons:

- The method of claim 1 generally results in a model for a mutually exclusive folding domain molecular switch including a fusion protein. However, while the specification does exemplify mutual exclusivity of ubiquitin and barnase domain folding [p.19], this example does not provide sufficient guidance drawn to mutually exclusive folding domain modeling of other fusion proteins. [Wands factors (2), (3), (8)].
- Methods for creating fusion proteins, loop insertion, and loop-entropy reduction are well-known in the art [Minard et al., Scalley-Kim et al.]. However, protein folding is still generally unpredictable. Despite the high level of skill in the art, one skilled in the art would not generally know what proteins should serve as the host protein, which "loop" sequences should be inserted into, or the energetic effects of loop insertion [Minard et al., p.129, col. 2] [Scalley-Kim et al., p.204, col. 2], therefore it would require undue experimentation by one of skill in the art to predictably practice the instantly claimed invention. [Wands factors (1), (2), (6), (7)].

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8, 9, and 10-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "a...molecular switch including a fusion protein comprising at least one insert protein....; and, a target protein...". As written, it is unclear whether the "molecular switch" consists of a "fusion protein" and a "target protein", or a "fusion protein" comprising an "insert protein" and a "target protein." It is unclear what is being claimed. Clarification is requested via clearer claim language.

Claim 1 recites an "amino-carboxyl length extending between an alpha carbon...is at least two times greater than an alpha-carbon-alpha carbon length". Applicant appears to be comparing distances between different alpha carbons. However, as written, it is unclear whether applicant is comparing the "length" of the two regions, or the physical distance between the two regions. Clarification is requested via clearer claim language.

Claim 1 recites the limitation "insert protein is operatively inserted...within at least one surface loop". As written, it is unclear whether the insert protein is inserted into the "surface loop" or through the "surface loop" (i.e. threading a needle). Furthermore, it is unclear as to the applicant's intended meaning of "operatively." What exactly is operating, the insert protein, the surface loop, or both? Clarification is requested.

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Claim 1 recites the limitation "a first surface loop" (line 5). Claim 1 later recites a "first surface loop amino acid" (line 6), therefore it is unclear whether "first surface loop" is referring to a particular type of amino acid, a position on the amino acid, a conformation, or otherwise. Clarification is requested.

Claim 1 recites the limitation "a second surface loop amino acid" (line 6). It is unclear whether "second surface loop amino acid" is referring to an actual "second loop", a position on an amino acid, or otherwise. Clarification is requested.

Claim 2 recites a "fusion protein." It is unclear whether this fusion protein is a virtual protein or a physical protein. Clarification is requested.

Claims 3-6, 8, 9, and 10-11 are rejected as they depend either directly or indirectly from claim 1.

PRIOR ART MADE OF RECORD

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Minard et al. (Protein Sci., 2001; 10, p.129-134)

Scalley-Kim et al. (Protein Sci., Feb 2003; 12, p.197 - 206)

Pack et al. (US 6,294,353; Issued: Sep. 25, 2001).

Olivia et al. (J. Mol. Biol., 1997, 266, p.814-830)

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CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ardin H. Marschel 4/27/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER